REMARKS

Claim 1 has been amended to correct a minor typographical error. Claim 24 has been added. Claims 7-23 have been withdrawn from consideration as being directed to non-elected subject matter. Upon entry of the above amendment, Claims 1-6 and 24 will be pending in the present application. Applicants respectfully submit that the addition of Claim 24 does not add any new matter within the meaning of 35 USC §132. Accordingly, entry of this amendment is respectfully requested. In view of the remarks set forth herein, further and favorable consideration is respectfully requested.

1. Rejection of claims 1-6 under 35 U.S.C. §103(a)

The Official Action states that claims 1-6 are rejected under 35 U.S.C. §103(a) as being unpatentable over You *et al.* (Journal of Immunology, 165:4581-4592, 2000) in view of Bout *et al.* (U.S. Patent No. 6,913,922). As the basis for this rejection, the Official Action states in relevant part:

> Because both You et al. and Bout et al. teach the use of retroviral and adenoviral vectors to transduce dendritic cells, it would be obvious for an artisan to substitute the retroviral vector taught by You et al. with the adenoviral vector taught by Bout et al, in order to arrive at a composition that can be administered to dendritic cells.
> Thus the claims are obvious.

Response

Applicant respectfully traverses this rejection of claims 1-6. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three

requirements. First, as the U.S. Supreme Court recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04-1350, 550 U.S. (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, supra, slip opinion at 13-15). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

A. Presently Claimed Subject Matter

The present pending claims as exemplified by independent claim 1 are directed to:

> 1. A composition comprising an adenoviral vector, wherein said adenoviral vector comprises:
>
> a) an adenoviral capsid, wherein said adenoviral capsid comprises subgroup B adenoviral capsid fibers selected from the group consisting of Ad11, Ad14, Ad16, Ad21, Ad34, Ad35, and Ad50; and
>
> b) a nucleic acid molecule, wherein said nucleic acid molecule comprises a retrogen cassette sequence encoding a retrogen protein, wherein said retrogen protein comprises:
>
> i) an antigen protein:
>
> ii) a leader sequence linked to the N-terminal of said antigen; and
>
> iii) a cell-binding domain linked to the C-terminal of said antigen protein.

B. You *et al.* (Journal of Immunology, 165:4581-4592, 2000)

You *et al.* describe a retroviral vector comprising a nucleic acid sequence encoding a fusion protein comprising VH leader sequence, HBeAg, and a Fc domain that can be administered to dendritic cells. However, You et al. do not teach or suggest an adenoviral vector or the inclusion of a subgroup B adenoviral capsid fiber in the viral vector as used in the presently claimed composition.

C. Bout *et al.* (U.S. Patent No. 6,913,922)

Bout *et al.* describe a recombinant replication defective adenoviral vector comprising a gene of interest operatively linked to a promoter and at least one adenovirus capsid protein from adenovirus serotype Ad11 or Ad35. *See* Bout *et al.* at

claim 1. In contrast to the presently claimed subject matter, Bout *et al.* do not teach or suggest that the gene of interest can be a retrogen cassette sequence encoding a retrogen protein comprising i) an antigen protein, ii) a leader sequence linked to the N-terminal of said antigen protein, and iii) a cell-binding domain linked to the C-terminal of said antigen protein.

D. No *prima facie* case of obviousness has been shown by the Examiner

The Examiner has failed to show a *prima facie* case of obviousness because there is no motivation to combine the teachings of the cited prior art references to arrive at the presently pending claims. Specifically, the skilled artisan would not be motivated to combine the retroviral vectors taught in the You *et al.* reference with the adenoviral vectors taught in the Bout *et al.* reference.

Recently, the Federal Circuit in ***Takeda Chemical Industries v. Alphapharm*, No. 06-1329, slip op. (Fed. Cir. June 28, 2007)**, has **applied the TSM test after *KSR***. The Appellant in this declaratory judgment action argued that the claimed chemical compound was an obvious modification of a previously known compound. *Id.* at 5. The Federal Circuit rejected this, holding that "in cases involving new chemical compounds, it remains necessary to identify some reasons that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound." *Id.* at 10. Notably, the Court also rejected the Appellant's "obvious to try" argument, as the Appellant failed to demonstrate that one of ordinary skill would have chosen the prior art compound to modify from the millions of possibilities. *Id.* at 15.

As outlined at page 15 of the present specification, the present subject matter is a combination of an adenoviral vectors expressing an adenoviral subgroup B fiber and a retrogen cassette, wherein the retrogen cassette is composed of a sequence encoding an antigen protein with a cell binding domain sequence at the C-terminus of the antigen and a leader/secretory sequence at the N-terminus of the antigen. In addition, these adenoviral vectors can be transduced into dendritic cells.

Accordingly, the presently claimed subject matter is directed to compositions comprising adenoviral vectors which comprise the subgroup B capsid fiber and the retrogen cassette. This composition is not taught or suggested independently anywhere in the cited prior art references.

In contrast, You *et al.* describe a *retroviral vector* system containing a fusion protein with a cell-binding domain and a leader sequence. You *et al.* do not describe that the retrogen cassette containing the antigen protein with the leader sequence and cell-binding domain can be inserted into an adenoviral vector system. You *et al.* show data using a retroviral vector system, and only a retroviral system.

Bout *et al.* do not cure the deficiencies of You *et al.* as Bout *et al.* describe an adenoviral vector system containing one adenovirus capsid protein and a gene of interest. Bout *et al.* do not describe the inclusion of a retrogen cassette to deliver the gene of interest in an adenoviral vector. Further, as described in the present specification at page 15, lines 12-18, because the antigen-presenting pathway to MHC-class I is distinctively different from that to MHC-II, it is difficult for an antigen to be presented to both MHC-I and II by DCs. However, the retrogen cassette technology allows presentation of antigens to both MHC-I and MHC-II as well as potently activating

Th, CTL and B-cells. Bout *et al.* lack this retrogen cassette insert and do not teach that their adenoviral vectors would present to both MHC-I and II. Therefore, the motivation to combine these references is clearly lacking.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-6.

E. The combination of references does not show a reasonable expectation of success and thus cannot render these claims obvious

The presently pending claims provide for more than the predictable use of prior art elements according to their established function. The present claims are drawn to compositions comprising adenoviral vectors which comprising the subgroup B capsid fiber and a retrogen cassette.

You *et al.* describe a retroviral vector system containing a retrogen cassette. Retroviruses by definition are *enveloped RNA* viruses. You *et al.* do not describe any other viral vector system that the retrogen cassette can be inserted.

Bout *et al.* describe adenoviral vectors that contain a subgroup B capsid fiber. Adenoviruses by definition are *nonenveloped DNA* viruses.

Therefore, a person of ordinary skill in the art would not reasonably expect that a retrogen cassette inserted into a retroviral vector would achieve the same effect as a retrogen cassette inserted into an adenoviral vector. As the adenoviruses are DNA viruses and retroviruses are RNA viruses, each has its own replication strategy and, in turn, each has different ways DNA is integrated into the host cell. One of ordinary skill

in the art cannot reasonably expect or predict that the same insert will function in the same manner and become integrated in the host cell in the same way using the two different viral vectors that themselves infect host cells differently.

Accordingly, the You *et al.* and Bout *et al.* references, taken alone or in combination, do not show a reasonable expectation of success by substituting one viral vector for another, and thus cannot render these claims obvious.

With regard to new Claim 24, the cited references, taken alone or in combination, do not render this new claim obvious, as has been argued above for Claims 1-6. In addition, neither the You *et al.* reference nor the Bout *et al.* reference teach the specific subgroup B capsid fibers recited in new Claim 24.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-6.

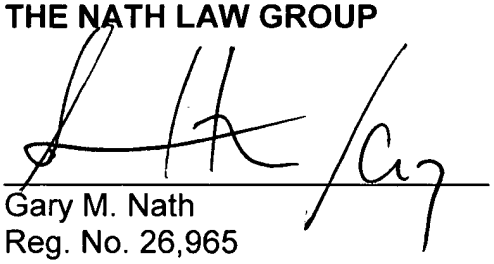
CONCLUSION

In view of the foregoing, Applicants submit that the application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



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